

We claim:

1. A pharmaceutical preparation comprising as a  
pharmaceutically active ingredient a compound wherein at least  
one of the hydrogen atoms is replaced with a deuterium atom or  
5 wherein at least one carbon, nitrogen or oxygen is replaced with  
a different isotope,

and a pharmaceutically acceptable carrier therefore.

2. The pharmaceutical preparation according to claim 1,  
wherein said compound is a member selected from the group  
10 consisting of anti-hypertensives, anti-hyperlipoproteinemics,  
anti-bacterials, anti-malarials, analgesics, cardiac medications,  
anti-arrythmic, anti-ulcer agents, and anti-fungals and  
immunosuppressive agents.

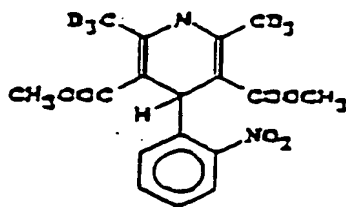
3. The pharmaceutical preparation according to claim 1,  
15 wherein said compound is a dihyropyridine.

4. The pharmaceutical preparation according claim 3, wherein  
said dihydropyridine is deuterated nifedipine having the formula

5. The pharmaceutical preparation according to claim 4, wherein at least one of the methyl groups of said deuterated nifedipine is  $\text{CD}_3$ .

6. The pharmaceutical preparation according to claim 4, wherein at least one of the methyl groups attached to position 2 and 6 of the dihydropyridine ring is substituted with  $\text{CD}_3$ .

7. The pharmaceutical preparation according to claim 6, wherein said deuterated dihydropyridine is deuterated nifedipine having the formula

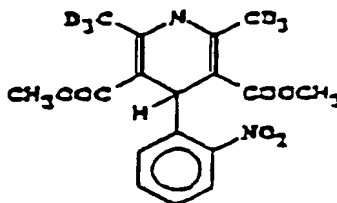


8. The pharmaceutical preparation according to claim 3, wherein said dihydropyridine is nifedipine, nicardipine, nimodipine, nivuldipine, nisoldipine, nitrendipine, felodipine, isradipine or amlodipine.

5 9. The pharmaceutical preparation according to claim 2, wherein said anti-bacterial is a member selected from the group consisting of ampicillin, methicillin, penicillin /Gd<sub>5</sub>, and penicillin V d<sub>5</sub>.

10 10. The pharmaceutical preparation according to claim 2, wherein said anti-bacterial is a member selected from the group consisting of amoxicillin, ampicillin, bacampicillin, pivampicillin, pivemcillinam, carbenicillin, piperacillin, ticarcillin and penicillin G.

11. Deuterated nifedipine having the formula



12. A deuterated compound, wherein the compound is selected from the list consisting of penicillin V, penicillin G, ricarcillin, cloxacillin, methicillin, piperacillin, cefaclor, cefmandole, cefazolin, cefotaxime, cefoxitin ceftazidime, gentamycin, tobramycin, amikacin, erythromycin, clindamycin, rifampin, minocycline, isoniazid, trimethoprin, sulfamethoxazole, ciprofloxacin, metronidazole, chloroquine, quinacrine, pyrimethamine, clotrimazole, ketoconazole, amphotericin, fluconazole, pentamidine, acyclovir, guancyclovir, didanosine, foscarnet, ganciclovir, amantadine, zalcitabine, zidovudine, aspirin, acetaminophen, ibuprofen, indomethacin, ketoprofen, sulindac, piroxicam, imuran, dexamethasone, prednisone, adriamycin, cisplatin, methotrexate, fluorouracil, cyclophosphamide, tamoxifen, L-dopa, benztropine, propranolol, sotalol, atenolol, acebutolol, isoproterenol, lidocaine, procainamide, quinidine, amiodarone, nifedipine, nicardipine, nitrendipine, diltiazem, verapamil, flunarizine, nitroglycerine, diisopyramide, furosemide, dobutamine, digoxin, ace inhibitors,  $\beta$ 2 agonists, short-acting nitrates, diazepam, alprazolam, lorazepam, amitriptyline, fluvoxamine, sertraline, fluoxetine, phenytoin, valproic acid, haloperidol, chlorpromazine, captopril, hydrochlorthizide, prazosin, etidronate, misoprostil, omeprazole,

ranitidine, cimetadine, dimenhydrinate, cisapride, Losec, metaclopramide, 5-aminosalicylate, glyburide, metformin, niacin, lovastatin, gemfibrozil, salbutamol, betamethasone, teophylline, and cyclosporin.

5 13. The pharmaceutical preparation according to claim 2, wherein said anti-bacterial is a member selected from the groups consisting of cloxacillin, flucloxacillin and nafcillin.

14. A method for making the deuterated dihydropyridine of claim 3, said method comprising:

10 dissolving a dihydropyridine in a mixture of deuteriochloroform and deuterium oxide to form a solution, adding trifluoroacetic anhydride and deuterioacetone to said solution, freezing and sealing said solution within a vessel, 15 heating said solution at a temperature and for a period of time sufficient to deuterate all of the hydrogen atoms at the 2 and 6 position on said dihydropyridine, and recovering said deuterized dihydropyridine.

15. A deuterated dihydropyridine made by the method of claim

14.

16. A pharmaceutical preparation comprising as the active component the deuterated dihydropyridine of claim 15 and a pharmaceutically acceptable carrier.

5 17. The method according to claim 14, wherein said deuterized dihydropyridine is deuterated nifedipine and said method comprises:

dissolving nifedipine in a mixture of deuteriochloroform and deuterium oxide to form a solution,

10 adding trifluoroacetic anhydride and deuterioacetone to said solution,

freezing and sealing said solution with a vessel,

heating said solution at a temperature and for a period of time sufficient to deuterate all of the hydrogen atoms at the 2 and 6 position on said nifedipine, and recovering said deuterized nifedipine.

18. The method according to claim 17, said method comprising:

dissolving 80 mg of nifedipine in a mixture of about 2 ml of

deuteriochloroform and about 0.5 ml of deuterium oxide to form a solution,

adding about 0.2 ml of trifluoroacetic anhydride and 2 ml of deuterioacetone to said solution and mixing therewith,

5 freezing and sealing said solution within a vessel,

heating said solution at a temperature of about 50° to about 65°C for a period of time of about 150 to 180 hours,

cooling said heated solution and recovering said deuterated nifedipine.

10 19. A deuterated nifedipine made of the method of claim 17.

20. A pharmaceutical preparation comprising as the active component the deuterated nifedipine of claim 19 and a pharmaceutically acceptable carrier.

21. A method for the treatment of hypertension in an animal  
15 suffering therefrom comprising administering to said animal a therapeutically effective amount of the deuterated nifedipine of the formula set forth in claim 3.

22. A method for the prolongation of the duration of action

of a drug comprising,

administering to a patient in need thereof a pharmaceutical preparation wherein the active ingredient thereof is a deuterated pharmaceologically active compound.

5 23. A method of detecting whether a pharmaceutical compound is identical and/or bioequivalent to a known pharmaceutical compound comprising the steps of

(a) determining the molecular and isotopic structure of said known pharmaceutical compound by isotope ratio mass spectrometry,

10 (b) determining the molecular and isotopic structure of said pharmaceutical compound subject to said detection by isotope ratio mass spectrometry,

(c) comparing the results of said two determinations to detect any isotope variation in the molecular structure of said  
5 pharmaceutical compound over that of the know pharmaceutical compound.

24. The method according to claim 23, further comprising converting said pharmaceutical compound to a gas, conveying said gas to an ionization source,

conveying a reference gas of known isotopic composition to



said ionization source,

measuring the abundance of at least two of  $^{13}\text{C}$ ,  $^{15}\text{N}$ , and  $^{18}\text{O}$   
for said pharmaceutical,

to thereby establish a two or three dimensional  
5 determination of said pharmaceutical compound.

25. A method of detecting whether a second pharmaceutical  
compound is identical and/or bioequivalent to a known  
pharmaceutical compound comprising the steps of

(a) determining the molecular and isotopic structure of said  
10 know pharmaceutical compound by isotope ratio mass spectrometry  
using formulae from the group consisting of

$$\delta^{13}\text{C}(\%) = (((^{13}\text{C}/^{12}\text{C}) \text{ sample} / (^{13}\text{C}/^{12}\text{C}) \text{ PDB}) - 1) \times 1000,$$

$$\delta^{15}\text{N}(\%) = ((^{15}\text{N}/^{14}\text{N} \text{ sample}) - (^{15}\text{N}/^{14}\text{N} \text{ standard}) / (^{15}\text{N}/^{14}\text{N} \text{ standard}) \times$$

15  $1000$ , and  $\delta^{18}\text{O}(\%) = ((^{18}\text{O}/^{16}\text{O} \text{ sample}) - (^{18}\text{O}/^{16}\text{O}$   
standard) / ( $^{18}\text{O}/^{16}\text{O}$ ) standard)  $\times 1000$ , wherein at least two formulae  
are selected,

(b) determining the molecular and isotopic structure of  
said second pharmaceutical compound by isotope ratio mass  
spectrometry using the same formulae selected in (a),

0 (c) comparing the results of said two determinations to  
detect any isotope variation in the molecular structure of said

second pharmaceutical compound over that of the known pharmaceutical compound.

26. The method according to claim 25, wherein said formulae selected are

5  $\delta^{13}\text{C}(\%) = ((^{13}\text{C}/^{12}\text{C}) \text{ sample} / (^{13}\text{C}/^{12}\text{C}) \text{ PDB}) - 1) \times 1000,$   
 $\delta^{15}\text{N}(\%) = ((^{15}\text{N}/^{14}\text{N} \text{ sample}) - (^{15}\text{N}/^{14}\text{N} \text{ standard}) / (^{15}\text{N}^{14}\text{N}) \text{ standard}) \times$   
1000.

27. The method according to claim 25, wherein said formulae selected are

10  $\delta^{13}\text{C}(\%) = ((^{13}\text{C}/^{12}\text{C}) \text{ sample} / (^{13}\text{C}/^{12}\text{C}) \text{ PDB}) - 1) \times 1000$  and  
 $\delta^{18}\text{O}(\%) = ((^{18}\text{O}/^{16}\text{O} \text{ sample}) - (^{18}\text{O}/^{16}\text{O} \text{ standard}) / (^{18}\text{O}^{16}\text{O}) \text{ standard}) \times$   
1000.

28. The method according to claim 25, wherein said formulae selected are

15  $\delta^{13}\text{C}(\%) = ((^{13}\text{C}/^{12}\text{C}) \text{ sample} / (^{13}\text{C}/^{12}\text{C}) \text{ PDB}) - 1) \times 1000,$   
 $\delta^{15}\text{N}(\%) = ((^{15}\text{N}/^{14}\text{N} \text{ sample}) - (^{15}\text{N}/^{14}\text{N} \text{ standard}) / (^{15}\text{N}^{14}\text{N}) \text{ standard}) \times 1000$   
and  $\delta^{18}\text{O}(\%) = ((^{18}\text{O}/^{16}\text{O} \text{ sample}) - (^{18}\text{O}/^{16}\text{O} \text{ standard}) / (^{18}\text{O}^{16}\text{O}) \text{ standard}) \times$   
1000.